CANCER AS A CHRONIC DISEASE*

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SCATTERED THROUGH the literature a series of remarkable cases indicates how unpredictable cancer is as a disease. In any series of untreated cases there will be certain ones with much longer survival than the average.[88] Some apparently show spontaneous disappearance either of the primary tumor or of secondary implants.[25, 31, 60, 80, 84, 90, 94] Some seem to grow in cycles with times of rapid growth alternating with stationary periods or actual recessions. And there is the phenomenon of delayed recurrence where the tumor reappears years later in the scar of the previous operation or in its immediate neighborhood. Sometimes the metastatic cells seem to have remained dormant in the lymph nodes or in organs of the body without ever producing symptoms. Sometimes after such a resting period the tumor cells seem to regain their vigor and flare up anew with rapid spread throughout the body. The balance between the growth rate of the tumor and the resistance of the host has been of interest to us for several years in the clinic as well as in the laboratory.

We have summarized cases which indicate that cancer may behave as a chronic disease. These cases cover a variety of cancers, showing that chronicity is not confined to any particular type.

* Read before the Southern Surgical Association, Hollywood, Florida, December 9, 1952.

CASE REPORTS

Case 1.—A. G. #12416, a 54-year-old man, entered the Strong Memorial Hospital on August 25, 1949. His medical history was a long one, involving many admissions to this and to other hospitals. His general health had never been good. In 1923 a gland was removed from the right side of his neck on the suspicion that it was a tuberculous lymph node. The microscopic picture was puzzling. Many pathologists studied the sections and a diagnosis of "metastatic tumor, source undetermined" was agreed upon. The late Dr. James Ewing thought that the most likely primary site was in the thyroid. Careful examination of the thyroid gave no indication of such a tumor at this time. The patient was referred to the Malignant Disease Institute at Buffalo, New York, where complete studies also failed to reveal a primary tumor. The neck area was treated by radiation, a total roentgen ray dosage of 1320 r being used.

He remained in fairly good condition following this until his first admission to the Strong Memorial Hospital on December 18, 1928. He felt weak and suffered from insomnia. Upon examination there were a few shotty glands in the cervical region and adenomas were noted in both lobes of the thyroid. The basal metabolic rate was −10 per cent. No surgery was advised by his attending physician.

He was next admitted to this hospital on February 28, 1932. At that admission bilateral inguinal hernias were repaired. The thyroid adenomas had enlarged and three were "shelled out," the largest being in the lower portion of the right lobe. This nodule measured 3.0 cm. in diameter. Microscopic sections revealed an adenoma of questionable malignancy. It had small irregular areas of calcification in it but there were atypical cells and it looked disorderly. It was called "probable malignancy." In April, 1932, he returned to the Malignant Disease Institute where he received 44,000 mg. hrs. treatment by radium pack.

B. M. R. taken in 1937 showed –30 per cent, accounting for his tiring easily. He had what was considered to be a coronary occlusion in 1941. He spent 3 months convalescing following this episode and did not have another attack until January 9, 1945. EKG showed only myocardial damage.

Late in 1948, it was discovered by his attending physicians that he had a very sensitive right carotid sinus reflex. Very light pressure over this area caused cardiac standstill and syncope. Pressure on the left carotid area had no effect. There were some small hard nodules felt in the operative scar over the right carotid sinus area. He had also lost weight and was discovered to have a mild glycosuria.

Consequently, right carotid sinus denervation was advised, and he entered the Strong Memorial Hospital on February 6, 1949. Attempts to abolish the reflex with atropine were only partially successful. At operation the right carotid sinus was denervated without incident and for 6 months the attacks were milder. Pressure over the right carotid area no longer produced the syndrome but the left carotid sinus became sensitive. Complete examination on August 25, 1949, showed no new developments except the cardiac standstill on pressure over the left carotid sinus. The B. P. was 124/80.

Therefore, left carotid sinus denervation was undertaken and the operation proceeded without trouble until the denervation was almost complete. Then the patient developd typical pulmonary edema. Following operation, he had a stormy course with labile blood pressure varying from 0 to 190 systolic and with labile pulse. His condition gradually improved, but on the second postoperative day he developed a right hemiplegia. The following day he had a quadriplegia and died quietly.

At postmortem examination there was a firm nodule to the right of the trachea a short distance above the manubrium. It measured 1.5 cm. x 1.5 cm., and cut with a gritty sensation. On microscopic examination this tissue was thyroid with dense collagenous fibers in which were wildly growing cords and nests of cells. These were present in two blood vessels, one of which appeared to be eroded. One parathyroid which was identified appeared to be normal.

The right lung had one small area of fibrosis which contained a small nest of cells with oval hyperchromatic nuclei and abundant blue cytoplasm. Some of these cells were in lymphatic vessels and a few had spread through the fibrous tissue.

The spleen weighed 40 Gm. Scattered throughout the parenchyma were hard yellow nodules varying up to 1.5 cm. in size. The liver weighed 1770 Gm. Scattered about on the surface and throughout the organ were firm, slightly raised, yellowish nodules which varied up to 2.0 cm. in size. Microscopic examination of both organs revealed the nodules to be metastatic thyroid carcinoma (Fig. 1).

An incidental unsuspected autopsy finding which may have been of importance in his death was a pheochromocytoma of the right adrenal. Multiple areas of myocardial infarction, thrombosis or embolism of the left middle cerebral artery and bilateral encephalomalacia were also present.

Summary. This man died following carotid sinus surgery and was found at autopsy to have thyroid carcinoma with metastases to lung, liver and spleen. The diagnosis of thyroid carcinoma had first been made 26 years previously, but no clinical evidence of malignant disease was present at the time of death.

Case 2.—This patient (A. H.), a 51-year-old female, was admitted to Genesee Hospital January 4, 1948, with a 2 year history of pain and a feeling of heaviness in the left thigh. Prior to admission, roentgenograms of the left femur demonstrated a circumscribed destructive lesion of the medullary portion of the lower shaft.

Her past history was of significance in that a subtotal thyroidectomy was done in 1935, and microscopic sections revealed carcinoma. She was given large doses of roentgen ray, producing a radiation myxedema for which she received thyroid extract daily.

Routine physical examination and laboratory studies were within normal limits. Roentgen rays of the rest of the skeletal system showed no other lesion.

A biopsy of the femoral lesion was done and revealed metastatic carcinoma of the thyroid. A tracer dose of radioactive iodine was given, revealing a slight uptake by the tumor area but not enough to warrant a therapeutic dose. Local resection with bone grafting was decided upon, reserving amputation as a second step if the original plan did not work. Accordingly, on April 25, 1948, the lesion was removed and the femoral shaft reconstituted with inlay tibial grafts from both legs.

She was in a hip spica for most of the next 9 months. Twenty-two months after operation she was crutch walking with weight bearing on the left leg. In February, 1950, a gland was noted on the right side of the neck. She was advised to have I^{131} and excision but refused. On March 4,

1952, she had low back pain and roentgenogram showed fracture. She had lost 50 pounds in weight and there were nodules under the skin of the neck, abdomen and flank.

Summary. Thirteen years after the primary tumor of the thyroid was removed, she was admitted with a painful thigh. The metastatic tumor had remained quiescent for 11 years and had slowly increased for another 2 years. She survived in good health for another two years following a second operation and then slowly developed widespread metastases.

Case 3.—V. S., #146696, a 46-year-old housewife, was admitted to the Strong Memorial Hospital on July 20, 1952. She had been a patient previously in December of 1938, suffering with hydronephrosis and nephroptosis on the right, and relaxed pelvic floor, rectocele and cystocele. On that admission it was noted that she had an enlargement in the right side of the neck and that she was extremely nervous. There was no tremor and her pulse rate was 84. Her kidney condition improved markedly on dilatation of the ureter with correction of the ptosis. She returned to India the following year and was not seen again until December, 1950. Her kidney condition showed very little change since the 1938 study.

On her hospital entry in July, 1952, she was concerned about lumps in her neck. She said that these lumps had increased slowly in size over the last 3 years. In 1938, a small lump was present in the region of her right mandibular angle. It was painless, asymptomatic, but gradually got larger, the increase being more rapid recently. In January, 1951, 3 nodules were noted in the neck and she was advised to have them investigated. She put this off for 1½ years before coming to the hospital on this occasion. During this time the nodules had merged into one mass in the right anterior triangle.

The thyroid gland showed many varying sized nodules, all hard and ranging from 0.5 to 2.0 cm. in diameter. On the left a chain of nodules was palpable along the anterior border of the sternocleidomastoid muscle. On the right there were two distinct masses of matted hard lymph nodes, the first located high, just below the angle of the mandible, the second involving the supraclavicular fossa area behind the sternomastoid. Each mass measured about 5.0 cm. in diameter and consisted of hard, spherical, nodular, non-tender, immobile tissue. A biopsy taken from the mandibular mass revealed metastatic papillary adenocarcinoma of the thyroid.

On July 25, 1952, a right hemi-thyroidectomy with a radical neck dissection was carried out. The removed thyroid was red-grey in color and contained numerous matted, firm, dark red nodes. On cut section these nodes were yellow, degenerated and contained old blood. In all the sections there were diffuse dense collections of pleomorphic tumor cells with oval and elongated pale hyperchromatic nuclei. For the most part these cells were arranged in a diffuse papillary formation (Fig. 2). In the upper pole of the thyroid there was an extremely hard nodule 1.5 cm. in diameter. This was considered to be the primary tumor. Convalescence was without incident.

She re-entered the hospital for radical dissection of the left side of the neck. The left side of the thyroid seemed uninvolved except for one small nodule which was found to be normal thyroid on frozen section. Accordingly, the left thyroid lobe was not removed. There were multiple nodules along the jugular vein, four of which contained metastatic papillary adenocarcinoma of the thyroid.

She had no complications and left the hospital in good condition on August 29, 1952. A test with I^{131} following operation showed no evidence of metastatic spread.

Summary. This patient was noted to have an enlargement in the right submandibular region on an admission here. She returned 14 years later, the mass having slowly enlarged to fill the entire right neck anteriorly and nodules being present on the left. Surgery at this time proved thyroid carcinoma with lymph node metastases.

Case 4.—G. S., #212059, a 58-year-old man was admitted to the Strong Memorial Hospital on December 6, 1943, with sciatic pain in his right leg. No treatment used by his physician gave relief except heat. Under this therapy there was a gradual decrease in the pain which had been present for approximately 3 months. One month previous to admission he noticed that there was a large swollen area on his right thigh. Roentgenogram showed an area of decreased density in the femur. He began to get about on crutches without weight bearing on the involved limb. There was only a vague aching pain in the region of the swelling. He had had no recent weight loss. His right kidney was removed for hypernephroma 16 years ago in 1927.

Examination revealed a large tumor mass in the upper part of the right thigh. It was firm, non-

FIG. 1

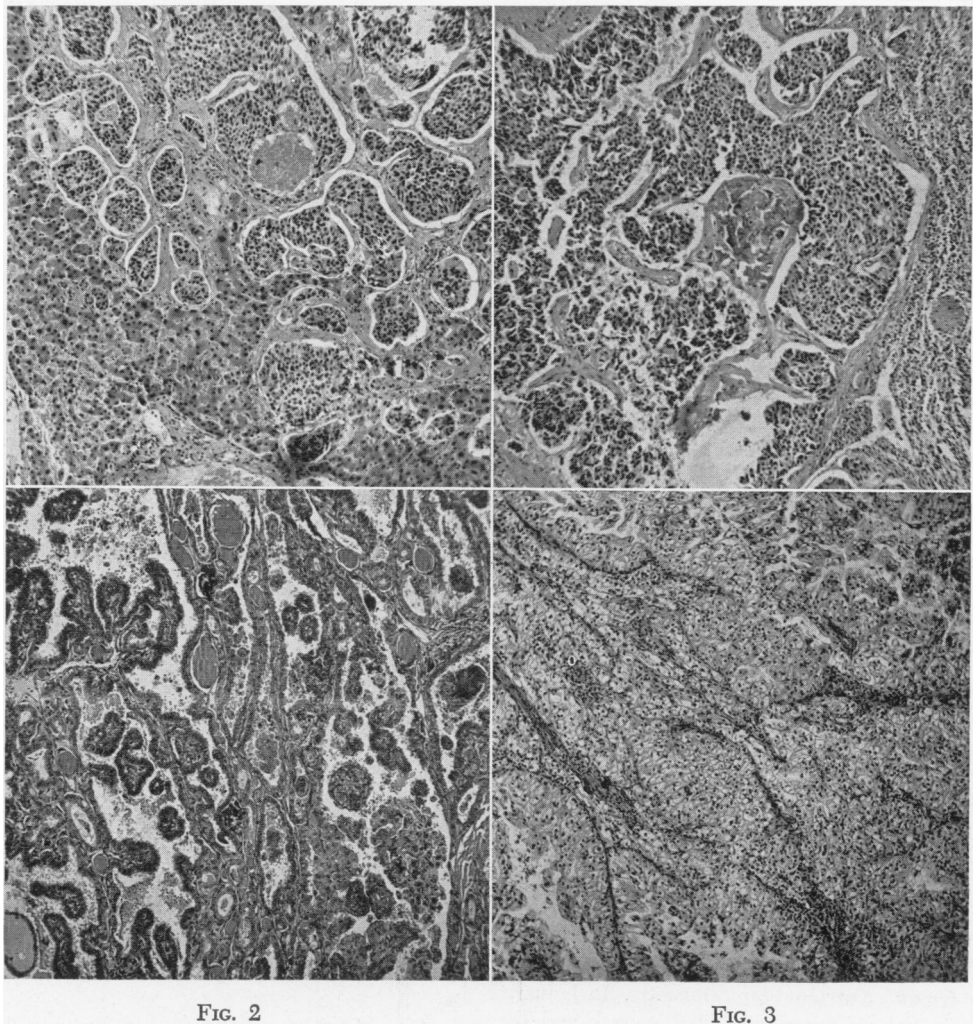

FIG. 2

FIG. 3

FIG. 1. A and B.—(Case 1) Thyroid carcinoma metastases to liver and to spleen (x 57).
FIG. 2.—(Case 3) Papillary adenocarcinoma of the thyroid (x 57).
FIG. 3.—(Case 4) Papillary carcinoma of the kidney with clear cells—metastasis in the femur (x 57).

tender and occupied the anterior, lateral and medial portions of the thigh. It measured 20 x 15 cm. There were no nodes grossly involved. Metastatic survey showed no other involvement.

Roentgenograms of the femur showed extensive areas of destruction of the cortex and central portions of the proximal end of the bone. There was a soft tissue tumor mass present with strands of irregular calcification. Biopsy showed typical clear cell carcinoma of the kidney (Fig. 3).

Following this a course of roentgen ray treatment was given over the tumor until 4100 r in air was attained.

Hip joint amputation was done on February 4, 1944, by Dr. Earle Mahoney. Healing was without incident. He did well following operation, gained in weight and after getting about on an artificial limb, discarded it and took to crutches entirely.

A note of September 13, 1952, from his doctor indicated that he had remained in good condition with no evidence of recurrence.

Summary. This man had a hypernephroma of the right kidney removed 24 years ago. It metastasized to the right femur and manifested itself 16 years after

his kidney removal. Following roentgen ray treatment and disarticulation of the femur, he has remained well for 8 years.

Case 5.—M. B., #99302. Patient was first seen in the O. P. D. here on February 12, 1935 at age 55, with history of lump in right breast of 5 weeks' duration. Examination revealed a small subcutaneous nodule 2 cm. in diameter on medial side of right areola. It was attached to the skin. Lesion was excised in O. P. D. under local anesthesia and the biopsy showed carcinoma of the breast. Patient was then admitted to the hospital and a right radical mastectomy was carried out on March 1, 1935. Microscopic sections showed more carcinoma, but no axillary lymph node involvement. A course of 500 r of roentgen ray was given. The wound healed slowly due to infection, but complete healing was present in 4 months. She had slight edema of the right arm but was without symptoms for the next 16 years, during which time she was followed in the O. P. D. In August, 1951, at age 71, she noted an ulcerated area under the right arm in the axilla. She returned to the O. P. D. on June 3, 1952, at which time the ulcerated area and one of several small crusted nodules over the anterior aspect of the right shoulder were biopsied. Both sites showed metastatic carcinoma (Fig. 4) and this responded very well to roentgen ray treatment.

Summary. Patient underwent radical mastectomy for carcinoma and was without signs or symptoms of recurrence for 16 years. Then she developed skin recurrence in the axilla and on the shoulder.

Case 6.—A. B., #269270, was a 69-year-old white female, first seen here in September, 1947, at which time she complained of a swollen left arm of 2 years' duration. In 1918, 29 years previously, she had a left radical mastectomy elsewhere. In 1930, 17 years previously, she had reoperation through same incision for "puffiness" at upper end of incision. Patient did not know what was done at the time. In 1945 she first noted slight swelling of left forearm which gradually increased and spread to upper arm. Eight months before first visit, she began to have pain and numbness in the arm as well. Examination revealed a swollen left arm with pitting edema and weak triceps.

In April, 1948, a stellate block gave relief of pain in the left arm so a left dorsal sympathectomy was done.

Some relief of pain was obtained but because of persistent swelling and disability from this, a left arm amputation was done in December, 1948.

In September, 1949, 31 years after the first operation, she was noted to have a small nodule in the left axilla which was thought to be scar tissue. However, biopsy was performed. The nodule proved to be a good bit larger than it appeared externally and could not be removed. Biopsy showed secondary carcinoma in skin of axilla (Fig. 5).

In January, 1950, she was admitted elsewhere with metastatic carcinoma in the liver and died in February, 1950.

Summary. A 40-year-old white female had left radical mastectomy in 1918. Twelve years later she had re-exploration and was then without symptoms until 1945, 27 years after original operation, when the left arm became gradually swollen and painful. First definite recurrence was discovered in 1949, and she expired in 1950, 32 years after first operation.

Case 7.—L. P., #7575, a 56-year-old female, was admitted to Rochester Municipal Hospital, June 1, 1927, because of recurrent breast cancer. She gave a history of right radical mastectomy elsewhere either 14 or 20 years before entry. Second operation for local recurrence 3 years later. She then remained without symptoms until one year before admission, at which time she noted 2 small lumps in the left axilla. Shortly thereafter another lump appeared below the scar of the second operation on the right. She had pain and weight loss for 6 months, but had worked up to time of admission.

Physical examination showed the scar of right radical mastectomy with a stony hard mass over the right costochondral junction at the third interspace and a larger hard mass in the left axilla. Roentgenogram showed metastatic spread through both lung fields.

The nodule on right chest was excised June 7, 1927, and showed carcinoma. She was given roentgen ray treatment with temporary improvement in symptoms.

On July 29, 1927, the mass was excised from left axilla and showed "carcinoma of breast, medullary in type" (Fig. 6).

There was a gradual downhill course. She was last seen here October 17, 1927. She died at County Hospital shortly thereafter.

Summary. Right radical mastectomy for carcinoma followed by local recurrence 3

TABLE I.

Reported by	Primary breast	Recurrence	Metastases	Time P. O.
Gougerot *et al*	case	locally	———	10 yrs.
Hartmann	4 cases	"	———	10 yrs.
"	3 cases	———	elsewhere	10 yrs.
"	case	locally	———	11 yrs.
Uffreduzzi (cit. Chilko)	case	"	———	11 yrs.
Brown	case #2	"	other breast axill. l. nodes	11 yrs. 6 mo.
Uffreduzzi (cit. Chilko)	case	"	———	12 yrs.
Hartmann	3 cases	"	———	12 yrs.
"	case	"	———	13 yrs.
Brown	case #1	"	axill. l. nodes	14 yrs.
Mortons	case	"	general	14 yrs.
Chilko *et al*	case	———	pleura, pericardium med. l. nodes	15 yrs.
Huguenin and Gillet	case	multiple nodules	———	15 yrs.
Hartmann	case	locally	———	15 yrs.
"	case	———	elsewhere	16 yrs.
Uffreduzzi (cit. Chilko)	case	locally	———	16 yrs.
Mortons	case	"	skin shoulder	16 yrs.
Gordon-Taylor	case #5	"	———	16 yrs.
"	case #4	"	———	17 yrs.
"	case #6	"	———	17 yrs.
Hartmann	2 cases	———	elsewhere	17 yrs.
Powers	case	locally	———	17 yrs. 6 mo.
Hartmann	2 cases	———	elsewhere	20 yrs.
Mitchell	case	locally	———	20 yrs.
Ficarra	case	———	generalized	20 yrs.
Ransohoff (cit. Powers)	case	locally	———	21 yrs.
Gordon-Taylor	case #1	"	———	21 yrs.
"	case #2	"	———	22 yrs.
Josephy	case	———	elsewhere	22 yrs.
Gordon-Taylor	case #3	locally	———	23 yrs.
Potherat (cit. Hartmann)	case	"	———	23 yrs.
Daland	case #2	" (22 ops.) many times	———	24 yrs.
Tod and Dawson	case	locally	opp. breast and axilla	24 yrs.
Perry	case	———	int. mamm. l. nodes mediastinum, pleura gall-bl. adrenals	27 yrs.
Boeckel (cit. Perry)	case	locally	———	29 yrs.
Mortons	case	"	———	29 yrs.
Verneuil (cit. Perry)	case	"	———	30 yrs.
Heurtaux (cit. Perry)	case	"	———	30 yrs.
Wallace (cit. Gordon-Taylor)	case	———	pelvic	30 yrs.
Steward (cit. Gordon-Taylor)	case	locally	———	31 yrs.
Bowlby (cit. Gordon-Taylor)	case	"	———	31 yrs.
Halsted (cit. Lewis and Rienhoff)	case	———	liver	32 yrs.
Mayo and Fergeson	case	multiple, local (10 ops.)	———	32 yrs.
Daland	case #1	locally	elsewhere	34 yrs. 6 mo.
Davidson and Ratcliffe	case	———	"	40 yrs.
Chauffard	case	locally	———	50 yrs.

years later. Then a period of either 10 or 16 years working and without symptoms followed by recurrence in right chest wall, left axilla, lungs, leading to death.

Case 8.—G. H., #327273. This 43-year-old female had the left eye removed elsewhere for malignant melanoma 8 years before being admitted here in May, 1951. She had been well until one month before admission when she noted some tearing from the eye and her prosthesis began to fit poorly.

Examination was not remarkable except for the left eye. In the socket there was a small mass of soft grey translucent tissue in the center of the orbital cavity. Roentgenograms of the skull, orbit and chest were negative.

A radical excision of the orbital contents with split thickness skin grafting of the orbital wall was

carried out uneventfully. The pathological specimen showed recurrent malignant melanoma.

Her postoperative course has been uneventful. A prosthesis with latex support for the lids has been fitted, and at present she is symptom free 1½ years after the second operation.

Summary. This woman had a recurrent malignant melanoma of the left orbit treated by radical excision 8 years after primary surgery. She is living and well, free from symptoms of disease, 1½ years following the second operation.

Case 9.—H. K., #120372. This patient was first seen here in October, 1936, at age 51, with history of pain in the left eye of 10 days' duration. The pertinent history dated back to a time 3 years before when he was brushed in the eye by a cow's tail while milking. He noted gradual loss of visual acuity from the left eye with complete blindness from it for about 9 to 12 months before admission. Ten days before admission he noted the onset of dull, aching pain in the left eye which rapidly became severe, so that he was hospitalized elsewhere, receiving supportive treatment until coming here.

Physical examination was not remarkable except for the left eye. The ocular tension was 48 as compared to 22 on the right, and the eye was totally blind. The cornea was steamy with the iris and lens displaced forward.

An enucleation of the eye was done after a dose of 740 r to the area, and the specimen showed a malignant melanoma of the choroid. Radium was implanted in the socket, and he received further roentgen ray therapy after discharge. There was discharge from the socket which cleared gradually and, when last seen in June, 1938, his condition was good.

He was lost to follow-up but was admitted to another local hospital in November, 1942, with an abdominal mass. Exploration showed multiple metastases in the omentum, and a biopsy revealed malignant melanoma. He died in March, 1943, and autopsy showed generalized melanomatosis.

Summary. This man had a 6-year period after enucleation of the left eye for malignant melanoma of the choroid. Then abdominal exploration revealed spread of the disease, and he died 6½ years after his original operation with generalized melanomatosis.

Case 10.—C. R., #182304. This patient was first seen here September 17, 1941, at age 35, because of a swelling in the left groin. For years he had had a small pigmented mole on the inner aspect of the left thigh, but about one year before being seen here this began to enlarge. The lesion was removed locally elsewhere in January, 1941, and again about 5 weeks later, the pathological report being non-pigmented melanoma. There was no further trouble until the groin mass was noted about 2 weeks before he was referred here. His general health was good and he was working as a carpenter.

Physical examination revealed a healthy white male with a firm 4 x 3 cm. mass in the subcutaneous tissues of the left thigh superior to the old surgical scar.

Radical block dissection of the left groin was carried out October 3, 1941. Pathological report was amelanotic melanoma of left inguinal nodes.

He was then well and returned to work. In July, 1942, a nodular indurated area was noted in the proximal thigh and admission for resection was recommended. The patient did not enter the hospital until November, 1942, at which time a recurrent nodule was removed from the skin of the left thigh. Another nodule was removed from the left thigh in January, 1943.

In January, 1944, he was seen again with 2 small nodules in the left thigh. He had been feeling well in the interim. The nodules were resected and proved to be further malignant amelanotic melanoma.

After this he felt well and gained weight. He was without trouble until a nodule appeared on the left buttock in October, 1946, and grew rapidly. This was excised in November, 1946, and proved to be a pigmented melanoma.

Another melanoma appeared on the neck and was removed in February, 1947. In March, 1947, another lesion was excised from the chest wall. In July, 1947, he was noted to have multiple areas of spread but, because these progressed slowly and left him feeling reasonably well, a lesion of the alveolar ridge was biopsied in October, 1947, and proved to be melanoma.

In January, 1948, he had resection of six lesions from the right forearm, left thigh, lip, chest wall, right ear and back in two stages. The lesion from the chest wall showed melanoma. The forearm and ear lesions showed pigmented nevi with questionable malignancy. The thigh and back lesions proved to be benign nevi and the lip lesion was diagnosed as epithelial hyperplasia.

In April, 1948, he was admitted comatose after five days of headache and died in a few hours.

Postmortem examination revealed metastatic melanoma to brain, heart, lungs, thyroid, multiple lymph nodes plus a recurrence in the original wound. There was intracerebral hemorrhage, including hemorrhage into areas of neoplasm.

Summary. Patient was first seen here at age 35 with malignant melanoma and was followed for 7 years with multiple excisions, remaining in good general condition for over 6 years after the lesion was first noted and expiring with widespread metastases.

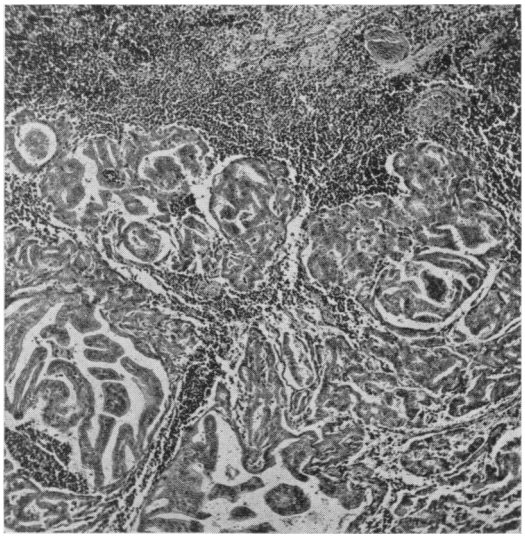

FIG. 4.—(Case 5) Carcinoma breast—metastasis in axilla (x 57).

Case 11.—M. L., #85609. This patient was first seen at Strong Memorial Hospital in February, 1934, at the age of 40. At that time she had a 4 cm. nevus removed from the left anterior chest wall. She gave a history of the lesion being present for several years with recent slow growth. Pathological report was pigmented nevus but the possibility was raised that the lesion was undergoing malignant degeneration (Fig. 7A).

In 1936, a right radical mastectomy was performed. On final pathological examination, the diagnosis was cystic mastitis with hyperplasia and acute inflammation.

She was then well with well controlled diabetes mellitus until February, 1939, when she noted a lump in the left axilla. On examination this lump was about 4 cm. in diameter and appeared attached to the chest wall. It was removed in April, 1939, and proved to be metastatic melanoma in the axillary nodes (Fig. 7B).

In September, 1939, she noted another lump in the left axilla and was readmitted for left radical mastectomy. Pathological examination showed no melanoma in the breast but metastatic melanoma was present in the axillary nodes.

About one month later she noted a swelling in the left neck and underwent left radical neck dissection in November, 1939. Pathological examination showed metastatic melanoma.

In February, 1940, a small necrotic metastatic node was removed from the left neck under local anesthesia. Another large mass of involved nodes was removed from this area in October, 1940, and a smaller mass excised in February, 1941. In June, 1941, a mass of involved nodes was removed from the right axilla and the neck was explored but only scar tissue found.

In July, 1941, she developed infection of the neck wound with drainage and attempted to commit suicide. At this time 1500 r was administered to the left cervical region in a 10 day period and 1600 r was given in September and October, 1941, for persistent swelling.

She improved slowly and by July, 1942, was symptom free and in good condition with no evidence of recurrence. Since that time she has had no evidence of disease and, now aged 59, she is living and well without evidence of melanoma.

Summary. This patient had a nevus removed from the chest wall in 1934, and axillary lymph nodes removed in 1939, which showed metastatic melanoma. During the next 2 years she had 6 operations with removal of involved tissue from the left axilla, left neck and right axilla. This was followed by 2 courses of roentgen ray to the left cervical region; for 10 years she has been free of symptoms or signs of melanoma.

Case 12.—E. F., #279416. This patient was first seen here April 26, 1948, at age 52. He gave the history that a tumor had been removed from the floor of his nose 6 years before admission. After the operation he received a course of roentgen ray therapy but 2 years later the swelling recurred and an extensive resection of the right maxilla was done. Two years following this operation the facial defect was closed with a neck flap and, since the right eye had dropped down when the supporting maxilla was removed, an enucleation was done. He was then well until shortly before being seen here when he noted a small swelling in his cheek.

FIG. 5

FIG. 6

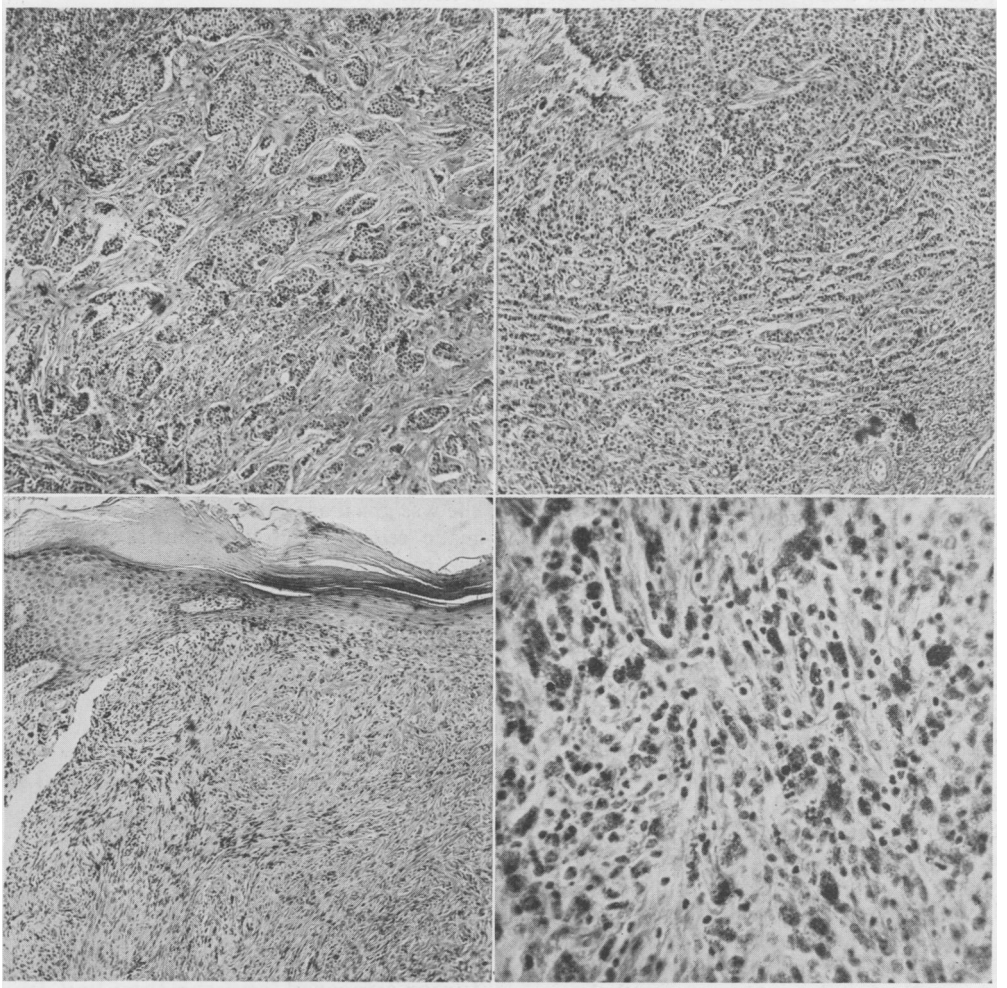

FIG. 7-A

FIG. 7-B

FIG. 5.—(Case 6) Carcinoma breast—recurrence in axilla (x 57).
FIG. 6.—(Case 7) Carcinoma breast—general metastases (x 57).
FIG. 7.—(Case 11) A. Malignant melanoma—subcutaneous (x 57).
B. Malignant melanoma—metastasis (x 146).

Examination revealed a well-developed and well-nourished white male whose right eye was missing. Below the region of the eye was a flap of grafted tissue and a palpable tumor was present just over the malar eminence. The right half of the hard palate was missing and through this defect the tumor nodule could be palpated bimanually. It was free of the skin and the mucous membrane of the cheek.

Roentgenogram of his chest was negative and the tumor mass was removed May 8, 1948. Microscopic sections showed a malignant cylindroma of salivary gland type.

He did well after this operation and a temporary prosthesis was made to fill the defect. He returned to work and felt well. In January, 1950, he noted a swelling on the right side of the nose and he was admitted February 13, 1950, for further surgery. Chest roentgenogram at this time showed bilateral pulmonary metastases with a large nodule in the right lung field and other nodules at the right hilum and at the left base. There were no pulmonary symptoms. The following day the nasal lesion was excised widely. Another local recurrence in this region was removed in May, 1950. On July 3, 1950, a more radical local oper-

ation, removing a block of soft tissue and bone, was done, the wound being packed open. Microscopic sections again showed tumor.

He continued to feel well and to continue full time work. A new temporary prosthesis was obtained and he returned in June, 1951, for plastic closure of the facial defect. Chest roentgenogram at this time showed slight growth of the metastatic nodules with the appearance of several new nodules. The facial defect was lined with a free split thickness skin graft and a pedicle graft from the forehead was used to close the defect externally. In July, 1951, the flap was severed and its base returned to the forehead. In February, 1952, another small nodule of recurrent tumor was removed from in front of the right ear. At present, he is working and feels well. He has no pulmonary symptoms, although chest roentgenogram (Fig. 8) shows further spread of the metastatic process.

Summary. This man has a malignant cylindroma, salivary gland type of 10 years' known duration with known bilateral pulmonary metastases for 33 months. He continues at full time work without pulmonary symptoms.

Case 13.—E. F., #261417. This patient was first seen here in March, 1947, at age 60 with the chief complaint of a recurrent tumor below the right ear. The pertinent history dated back 22 years. At this time she first noticed a small swelling under the right ear which gradually enlarged until 4 years later it was removed locally in a doctor's office. The tumor recurred and a second removal was done 2 years later. She was then without symptoms for about 12 years until the mass gradually recurred. Four years before admission, reoperation was done with roentgen ray therapy before and after operation. Another local operation was done 2½ years before admission, and a right facial paralysis followed this operation. For the next year she was well, and then gradually began to have local pain for the first time. A large recurrent mass was excised elsewhere 6 months before admission. At this time all tumor was not removed, and the wound never healed completely.

On admission here she presented a raised, ulcerated 4.5 x 4.0 cm. mass just anterior to the right ear and a complete right facial paralysis was present. No definite cervical lymphadenopathy was present. A chest roentgenogram showed bilateral metastatic lesions.

A radical removal of the local lesion was done March 20, 1947, leaving an open wound extending through the temporal muscle and exposing the ascending ramus of the mandible. The pathological specimen showed carcinoma of the parotid gland with extension into the ear lobe and local lymph node metastases.

In April, 1947, a small nodule was removed from the lower margin of the granulating wound, and a split thickness skin graft was applied. The wound healed well except over the exposed mandible where the graft did not take. By late May, 1947, a recurrence was obvious in this area, and in June and July she received 6000 r of roentgen ray therapy. There was a dramatic regression of the local tumor although the wound never healed completely. In November, 1947, chest roentgenogram showed a considerable increase in size and number of metastatic nodules in both lung fields and the patient was beginning to notice bronchial difficulty. The ulcerated area over the mandible gradually increased in size and in March, 1948, she was given another course of 5700 r for symptomatic relief. Again the ulceration decreased in size temporarily.

When last seen in October, 1948, she was noted to have a small new area of tumor above the ear with the ulcerated area persisting as before. It was noted that she was getting along reasonably well at home, being bothered largely by a cough which was relieved by codeine. She died at home in February, 1949, at which time her physician felt she had abdominal and perhaps central nervous system metastases.

Summary. This patient had a carcinoma of the parotid gland with symptoms first noted 24 years before death. Operations were done locally 4 and 6 years after the tumor appeared, and she then had 12 years without symptoms before recurrence occurred. There were known bilateral pulmonary metastases during the last 2 years of life.

Case 14.—M. O., #223199. This 45-year-old woman came into the Strong Memorial Hospital in September, 1944, with obstruction of the ileum. At operation she was found to have a tumor 2 feet from the ileo-cecal valve, encircling the bowel. There were many small metastases in the mesentery, in the pelvis, in the peritoneal *cul de sacs* and in the uterus. Several small nodules were present also in the liver. A lateral anastomosis was made, side-tracking the obstructed bowel.

Microscopic sections revealed that the tissue was an argentaffine tumor, metastatic in the lymph nodes.

She recovered well from the operation and remained symptom-free until March, 1946. Then she had gas pains and loss of weight. Masses could be felt in the right lower quadrant and in the right *cul de sac*. A lateral anastomosis was made between the lowest dilated small intestine and the transverse colon. The whole peritoneal cavity was studded with nodules from pin-head to buck-shot in size.

She slowly declined with loss of weight and strength and frequent attacks of abdominal pain, requiring opiates for sedation. Distention and vomiting were troublesome also. Palliation with drugs was fairly successful. She expired on October 4, 1948.

Summary. A woman with advanced carcinomatosis involving the abdominal contents survived in fair comfort for 2 years during which she worked as a secretary. For 1½ years following this she had increasing difficulty and required opiates for relief.

TABLE II.

Reported by	Primary malignant melanoma	Recurrence	Metastases	Time P. O.
Schroeder	r. eye	———	liver	6 yrs. plus
Mortons	case 9, l. eye	———	viscera	6 yrs. 6 mo.
Mortons	case 8, l. eye	loc. 8 yrs.	———	9 yrs. 6 mo.
Lilley	r. eye	———	liver (19 lb. 6 oz.)	10 yrs.
Dobbertin	l. eye	———	cerebellum, sp. cord	10 yrs.
Wilbur and Hartmann	case 9, eye	———	liver, subcutaneous	10 yrs.
"	case 10, eye	———	lungs, bones, subcutan.	10 yrs.
Hutchinson (cit. Schroeder)	eye	———	liver	11 yrs.
Marshall (disc Fisher and Box)	eye	———	loc. (not stated)	11 yrs. 5 mo.
Wilbur and Hartmann	eye	———	liver, subcutaneous	13 yrs.[4]
Fisher and Box	eye	———	liver (12 lb. 6 oz.) parietal pleura myocardium, l. ventricle	14 yrs.
DeCoursey (cit. Hall)	eye	———	viscera	16 yrs.
Lawbaugh	eye	———	liver	17 yrs.
Webb-Johnson and MacLeod	eye	———	chest wall, 6-7 ribs, pleura	18 yrs.
Cairns	l. eye	———	r. scapula	18 yrs.
O'Brien and Gray	l. eye	———	liver	18 yrs.
Ginsberg (cit. Hall)	eye	———	viscera	24 yrs.
Albers (cit. Ewing)	l. eye	———	th. spine, sp. cord, lungs, liver, heart l. nodes	24 yrs.
Hall	l. eye	encapsulated rec. l. optic n.	Liver, lung, vena cava, adrenals	30 yrs.
Wilder	eye	———	liver, viscera	32 yrs.
Hutner	r. eye	———	breast 26 yrs.. neck 34 yrs.	d. 36 yrs.
Mortons	l thigh	———	l ing. nodes, multiple skin	6 yrs. plus
Reyes and Horrax	1 shoulder	———	l axilla 15 mo.	7 yrs. 9 mo.
			l. frontal 2 yrs.	1 & w to date
Wilbur and Hartmann	case 5 l. face	several local	brain, behind left ear	10 yrs.
"	case 7 l. arm	———	heart, spleen, stomach, liver, lung, int. mesentery, l. nodes	10 yrs.
Eve	hand	———	axilla	11 yrs.
Wilbur and Hartmann	case 4 cheek	local	lungs, intracranial sinuses	12 yrs.
Mortons	chest wall	———	r. axilla 2 yrs.	16 yrs.
			l. axilla 5 yrs.	1 & w 10 yrs.
			l. neck 5 yrs.	without
			r. neck 6 yrs.	rec. or met.
Eve	hand	1st 10 yrs. 2nd 20 yrs.	axilla	20 yrs.
Chauvin	face	4 x locally	———	22 yrs.

Case 15.—J. H., #231244. This patient, a 52-year-old male, was first seen here in April, 1945, with a chief complaint of hemorrhoids of 9 months' duration. History revealed that he had had gradual enlargement of his abdomen over a 20 year period, with a considerable increase in the preceding 9 months.

Examination showed a chronically ill man with a tremendously distended abdomen containing fluid. A rectal prolapse was present.

He was admitted for study and by abdominal paracentesis 11,500 cc. of cloudy, green fluid were removed. After this an elongated upper abdominal mass was palpable. Gastro-intestinal roentgenograms and barium enema showed no intrinsic lesion.

An exploratory laparotomy was performed May 15, 1945. About 2 liters of straw colored fluid escaped. Exploration revealed extensive carcinomatosis of visceral and parietal peritoneum with the omentum completely replaced by tumor and tumor nodules in the hepatic capsule, but not obviously in liver substance. A mass of tumor was palpable posterior to the stomach, and it was felt that the primary was probably in the pancreas. The diagnosis was confirmed by biopsy (Fig. 9). His postoperative course was uneventful, although a small amount of fluid accumulated in the abdomen.

He was lost from sight but returned July 26, 1948, complaining of hemorrhoids. He had been active and feeling well in the interim. At this time multiple masses were palpable throughout the abdomen, but little fluid was present. He continued to do fairly well but began to develop anorexia. An abdominal paracentesis was done in May, 1949, and 3700 cc. of cloudy, greenish fluid removed. The spun sediment showed many carcinoma cells. He went slowly down hill and died at home January 17, 1950, almost 5 years after his operation.

Summary. This patient lived for almost 5 years after demonstration of a histologically proven carcinomatosis of the peritoneal cavity. During most of the time he was active and in reasonably good health.

Case 16.—J. C., #32829. This patient was first seen here March 3, 1930, because of abdominal discomfort. At this time he was a 58-year-old male who had had a sense of abdominal fullness with weight loss 4 years before admission. A gastro-intestinal series was negative, and the symptoms were relieved by bicarbonate of soda. He was well until 10 months before admission when symptoms recurred, but examination elsewhere was not revealing. The symptoms subsided and he returned to work only to have recurrence one month before admission. At this time the abdomen began to enlarge, and his appetite decreased due to abdominal bloating. There were no other gastro-intestinal symptoms.

Examination revealed an emaciated male appearing chronically ill. The lower abdomen was distended with fluid present and an irregular, hard, movable mass filled the right lower quadrant extending beyond the midline to fill the medial upper quarter of the left lower quadrant. Rectal examination was negative.

A stool specimen was negative for occult blood, and upper gastro-intestinal series, barium enema and chest roentgenogram revealed no evidence of malignancy.

A biopsy of a small intraperitoneal nodule was carried out under local anesthesia. The mass was jelly-like in consistency, and microscopic sections showed colloid in peritoneum from colloid cancer.

He received a series of ultraviolet treatments to the abdomen and during the next few months the abdomen decreased in size. The patient went back to work. In October, 1930, he was readmitted because of recurrence of fluid. It was felt that the diagnosis of carcinoma was not certain so, after another series of negative roentgenogram studies, an abdominal exploration was undertaken November 5, 1930. When the abdomen was open, 4700 cc. of fluid were evacuated and it was discovered that the entire bowel was matted together by gelatinous tumor. This mass involved the stomach and gallbladder, and the liver was studded with nodules. Biopsy showed colloid carcinoma.

He did well and went back to work. An abdominal paracentesis was done in February, 1931, and 6 liters of fluid removed. On microscopic study there was no evidence of glandular tissue in the sediment of this gelatinous fluid. He again did well and returned to work, gaining weight and strength.

He was readmitted in September, 1932, with symptoms of low grade intestinal obstruction. The symptoms subsided on conservative treatment, and he again returned to work.

In January, 1933, abdominal distention again became annoying. An attempt to remove fluid through a large trocar was unsuccessful, so a small incision under local anesthesia was employed. The fluid was discovered to be gelatinous, containing tissue masses, and was difficult to evacuate. Pathological study of the tissue masses showed colloid material without cell structure.

In September, 1933, he was still doing daily work although his abdomen was tremendously swollen and there was edema of the legs. He was placed on a salt free diet and given ammonium chloride intermittently. He went gradually downhill, losing weight until he was admitted in terminal condition October 2, 1934. He died shortly after admission and autopsy showed colloid carcinoma involving the entire peritoneum. The primary site could not be determined.

Summary. This patient was found to have extensive colloid carcinomatosis of the peritoneum and liver for 4½ years after the original diagnosis was made. During at least 3½ years he continued full time work and had very little discomfort despite a tremendously enlarged abdomen.

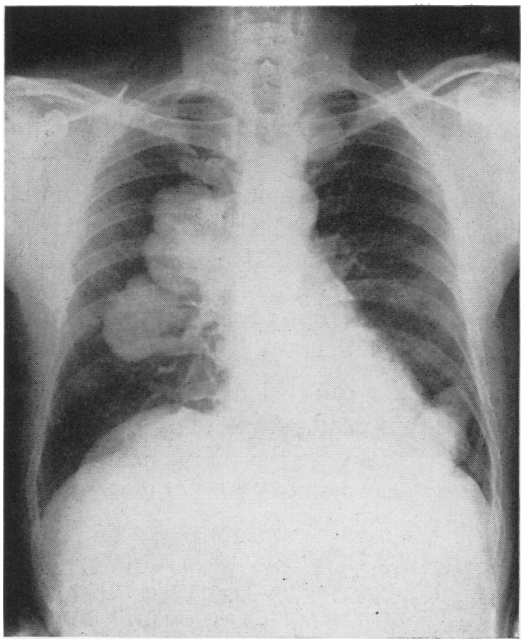

FIG. 8.—(Case 12) P. A. chest roentgen ray with bilateral pulmonary metastases.

Case 17.—A. M., #14432, a 42-year-old woman, was admitted to the Strong Memorial Hospital in April, 1928, complaining of pain in the left upper abdomen. It began one year before and steadily increased in severity. She lost 40 pounds in weight. A mass appeared in the left upper quadrant and grew slowly in size. She lost her appetite and had vomiting attacks on several occasions. There had been a fever ranging from 102° to 103° for the last 3 months. In her past history she had had metrorrhagia 8 years before. This was controlled by roentgen ray therapy, which produced an artificial menopause.

On entry her temperature was 103°, pulse 120 and blood pressure 145/85. Considerable weight loss and anemia were evident. A smooth, firm, sharply-defined, somewhat tender mass, which descended on inspiration, was present in the left upper quadrant. It could also be palpated in the left lumbar region. No notch was felt.

Laboratory examinations showed a trace of albumin and many casts in the urine. Roentgen ray examinations showed a high left diaphragm. The stomach was pushed medially, the transverse colon and splenic flexure were displaced downward. Position of the left kidney was not determined.

A retroperitoneal tumor weighing 1550 Gm. was removed on April 7, 1928. Pathologic study showed it to be an adenocarcinoma of the adrenal.

She regained her weight and did very well for 3 years following operation, when she had a recurrent tumor weighing 300 Gm. which was removed in June, 1931. Following this operation she was carefully followed. She developed severe hypertension with blood pressure 220/130, but with scarcely any symptoms. Her next recurrence was removed in June, 1938. The tumor weighed 270 Gm. Her blood pressure fluctuated within rather wide limits following operation—from 120 to 175 systolic and from 80 to 100 diastolic.

In September, 1938, her fourth recurrence necessitated a resection of the transverse colon with an end-to-end anastomosis. The tumor grew directly through the intestinal wall to form a mass within the lumen. During the winter her hypertension returned with blood pressure measuring 250/130. A course of 3000 r roentgen ray therapy was given.

In June, 1943, at exploration, the tumor was diffusely scattered through the upper abdomen without definite margins. She lost weight, felt fatigued, and had attacks of distention. She improved somewhat following treatment with diethylstilbesterol.

During the next 3 years she varied in weight and appetite. She lost and gained according to her ability to eat. Her bowels were irregular, sometimes being constipated and at other times very loose. In April, 1946, she had an almost complete obstruction, which was relieved by a lateral anastomosis. When last seen in the clinic, June 24, 1946, she was thin but feeling better than she had in years. No definite masses could be made out, although there was a sense of increased resistance in the left upper quadrant. On June 27, 1946, while at home, she suddenly felt faint, went to bed and died within a few minutes. No pathologic examination was obtained.

Summary. This patient lived for 18 years with a known extensive adrenal carcinoma and the neoplasm was probably not responsible for her death.

DISCUSSION

Cases 1, 2 and 3 are excellent examples of metastatic cancers which have then quieted down. Metastasis has been regarded as evidence that a cancer is really

malignant,[39] and yet in all three instances cited the metastatic tumors have temporarily lost their malignant character. In Case 1 there was nothing to lead to a suspicion that cancer still persisted and the autopsy findings were a great surprise to all the attending physicians. Case 2 manifested itself by bone pain, but over a period of many years this group of metastatic cells smouldered like a spark in damp surroundings. The metastasis to the submaxillary area was already established when Case 3 was first examined. This submaxillary node is a frequent early metastatic site for papillary adenocarcinoma of the thyroid, as has been noted by us on several previous occasions. It is notable that the primary growth in the thyroid could not be detected by the methods of physical examination in any of these cases. It has been difficult on other occasions to demonstrate the primary thyroid tumor. This is probably due to the fact that the primary lesion at times is tiny—measuring only a few millimeters in diameter, that it is often deep in the lobe or isthmus, and that frequently it occupies a posterior position.

Hirsch and Miller[45] reported three cases of thyroid malignancy with long survival, one in a female child aged four, who had metastases to the lymph nodes at the time of removal of the right lobe and isthmus. She survived for 6 years and died with pulmonary metastases. The second case, a 29-year-old male, following some unsuccessful attempts to remove the thyroid and the metastatic nodules, had recurrence in the nodes of the right neck 9 years later and lived with the disease for 17 years. The third patient, a 27-year-old male, had metastatic nodules appear successively for several years, but at last report was living and well 15 years after the appearance of the first metastatic node.

Basset[7] reported a woman of 56 who had a small tumor of the left lobe of the thyroid, very slowly developing and completely latent. She had a metastasis to the left femur, which was excised, a bone graft being substituted, and roentgen ray treatment given. A hemithyroidectomy was also followed by roentgen therapy. For four years she remained in perfect health. Then, a new metastasis was discovered in the right tibia and on a skeletal survey a completely latent unsuspected metastasis in the skull was found. These two new areas were treated by removal followed by roentgen ray therapy. Microscopic sections from the thyroid showed papillary adenocarcinoma. But all three bone metastases appeared to be normal thyroid without any sign of malignancy. In the literature this is referred to as benign metastasizing goitre. Basset prefers the designation "cancer latent metastasizing."

Case 4 illustrates the bizarre character o the kidney cancers. These lesions are notorious for the queer localizations of their metastatic spread. Apparently one metastatic focus may be the only spread in certain cases as removal of it is followed by a healthy period of years as in our case. Clairmont[19] reported a similar instance where the metastasis was at the bifurcation of the trachea and did not manifest itself for ten years after removal of the kidney. It then perforated into both right and left bronchi, causing the death of the patient. Broster[12] reported a case similar to ours where spontaneous fracture of the femur occurred nine years after nephrectomy. After amputation, the 72-year-old woman was discharged "fit." Graves and Mabrey[38] noted recurrence in the scar and lumbar area 20 years after removal of the kidney adenocarcinoma. Deming[23] had two of his patients with hypernephroma die of metastases (site not stated) after 10½ and 11½ years respectively. Stortebecker[93] removed a metastasis from the right cerebellum one year after right nephrectomy for hypernephroma. The patient was living in reasonably good health, with slight ataxia and some impaired vision 14 years after the brain operation. Starr and Miller[91] removed a solitary jejunal metastasis 20 years after the nephrec-

tomy for a clear cell carcinoma. Barney and Churchill,[5] combined in a nephrectomy for the primary tumor and a lobectomy for the solitary metastatic lesion, the patient still surviving after 20 years of excellent health (information courtesy of Doctor Churchill). Instances of long evolution of kidney tumors 19 years[26] and 20 years[85] indicate the resistance to growth in some cases. Salm and Pollok[86] reported a six and a half year survival of a patient with a hypernephroma and a spontaneous humerus fracture. No treatment other than stilbestrol was given as the condition was considered unsuitable for definitive measures.

At one time cancer of the breast was considered cured if no recurrence or metastasis was evident after three years. The time was later extended to five years. There were so many exceptions even then of late recurrence in the scar or late metastases that it is now customary to speak of survivals rather than cures. For this reason, the surgeon must keep his cancer patients under continued surveillance. We present three instances of long survival with recurrence or metastasis in Cases 5, 6 and 7. Table I summarizes cases of breast cancer from the recent literature with local recurrence or metastasis over 10 years after primary surgery.

Cases 8, 9, 10 and 11 are good examples of the vagaries of malignant melanotic growths. These tumors may be among the most rapidly fatal of any of the malignancies, but the occasional exceptions are always unexpected and welcomed. The melanotic malignant tumors of the eye are well known for their late metastases, usually to the liver. But almost every organ may be invaded by these growths. Multiple metastases to the liver may look like a "mass of blueberries."[87] In Lilley's case[58] the liver became a huge coal-black organ weighing 19 pounds 6 ounces. The exceptional metastasis to the scapula reported by Cairns[15] reminds us that the two commonest sites of metastases for the melanotic tumors of old grey horses are the rhomboid muscles and the parotid. The case reported by Reyes and Horrax[82] where a large metastatic melanoma was removed from the left frontal lobe indicates that even such desperate attempts are worthwhile at times. This patient is still alive in apparent good health, five years and nine months after the brain operation (information courtesy of Doctor Horrax). Our Case 11 shows a similar response. After six years of repeated operations, two radical mastectomies and two radical neck dissections, the patient has remained in excellent health for the last 10 years, 16 years since her original operation. Table II summarizes cases of malignant melanoma from the recent literature with long periods of freedom before recurrence or metastasis occurred.

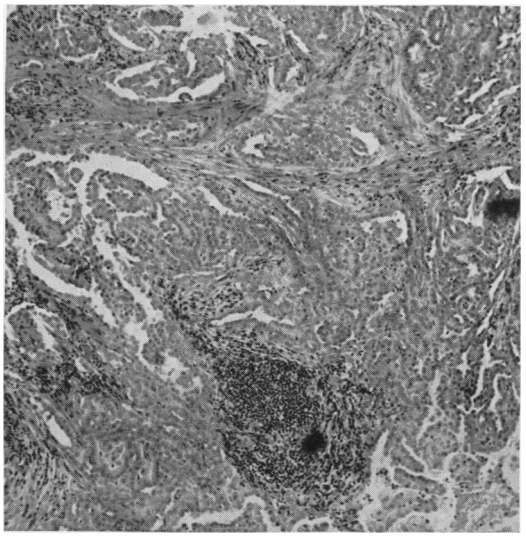

FIG. 9.—(Case 15) Adenocarcinoma pancreas—peritoneal metastases (x 57).

Cases 12 and 13 are of interest in that both patients had extensive bilateral pulmonary metastases for a period of years with few pulmonary symptoms and little systemic reaction. It is well known how slowly the mixed tumors of the salivary glands evolve. Some authorities consider them essentially benign. Every surgeon fears that he may do an incomplete oper-

ation or break through the capsule in operating on these tumors with resulting recurrence. Marshall and Miles,[61] commenting on the duration of mixed tumors in their series, noted that 29 had been present from 6 to 15 years; that 12 had grown slowly for from 16 to 26 years; and that 10 had been present for over 26 years.

Recurrences occurred in one of their patients in nine years and in two others in 11 years following excision. They state that recurrences of benign salivary gland tumors have been reported as late as 47 years after excision. Mulligan[65] reviewed the metastasis of salivary gland tumors, reporting his own case of left parotid cancer which after 11 years grew rapidly from pea to lemon size, causing death in the 12th year, with widespread metastases to viscera and bones. He cites a similar submaxillary case of Barozzi and Lesne of 12 years' duration, a cylindroma with metastases to cervical and tracheal lymph nodes and lungs.

Griffini and Trombetta[40] likewise had a cellular mixed tumor of the submaxillary gland which metastasized after 16 years to the cervical and bronchial lymph nodes, pleurae and lungs. Partsch's case[71] carried a right parotid mixed cylindroma for 16 years, with two recurrences and metastases to the pleurae. Brunschwig's patient[14] with a "mixed tumor" of the sublingual gland had one recurrence and died with metastases to the lungs and pleura after 19 years. LeDentu's woman of 61[55] allowed her parotid tumor to grow for 30 years until it reached half the size of her head. At postmortem it weighed 1300 Gm. There were metastases in the lungs, liver and meninges.

Livingston's right parotid teratoma[59] had been present nine years and recurred six years after operation. At postmortem there were widespread metastases. From the Mayo Clinic, Quattlebaum *et al.*[79] reported four cases of cylindroma of the parotid, Case 11 living eight years with 10 recurrences after local excision and radium; Case 12 living seven years with six recurrences after parotidectomy and radium; Case 13 living seven years following local excision and radium, the last recurrence being four years previously; and Case 14 living 15 years with two recurrences following parotidectomy and roentgen ray treatment. This gives an indication of the unpredictable behavior of these adenocarcinomas.

Truffert[96] did a supposed total parotidectomy only to have a recurrence 16 years afterwards. He operated a second time 18½ years after the first attempt and commented that a parotidectomy is not complete unless the inferior wall of the cartilaginous auditory canal is removed.

Baclesse[3] followed nine mixed tumors and nine cylindromas for 20 years at the Curie Institute. Whereas the mixed tumors rarely had visceral metastases, seven out of nine of the cylindromas metastasized. These metastases occurred in the pleura and pulmonary areas, associated twice with osseous metastases. The metastases came late, without clinical signs and passed unperceived unless shown by chance roentgenograms of the chest. Metastases appeared in the 22nd year of the disease in Case 1 following several recurrences. Case 2 had a succession of recurrences with death from silent pulmonary metastases in the 12th year. Cases 4 and 5 had many pulmonary metastases without a single pulmonary sign in their 13th year of disease. Case 6 went ten years before diffuse involvement of the lungs. Case 8 was that of a mixed tumor of the parotid which had repeated operation alternating with roentgen ray treatments. She finally succumbed to pulmonary metastases 21 years after appearance of the tumor.

Cases 14, 15 and 16 indicate that diffuse involvement of the peritoneum and viscera is not necessarily rapidly fatal. The patients may have several years of fairly comfortable, productive existence. Case 17, during the 18 years following her first operation, had an adenocarcinoma of the left adrenal which remained localized in the left upper

abdomen. Although growing quite large and recurring repeatedly with local invasion, this tumor never showed evidence of metastatic spread. The patient remained comfortable throughout this long period, except when the local growth necessitated surgery for bowel obstruction.

Although we have no cases in these groups, there are reports in the current literature of long survivals in patients with cancers originating in lung, bone, uterus, ovary, stomach, intestine and testis. Goldman[34] reports 11 cases of lung cancer with an average survival untreated of 7½ years from onset of symptoms to definitive diagnosis. Included in this group are individual cases of 20, 14 and 12 years' duration. According to Ewing[28] highly osteoid tumors may pursue a very chronic course. He cites Paget's[70] and Holmes'[46] cases with fatal metastases 21 and 25 years respectively, after onset of disease. Jenckel's patient[52] died of pulmonary metastases 15 years after amputation of the femur for osteogenic sarsoma. One of Badgley and Batts' patients[4] had an exactly similar course.

Liavaag[57] reports a patient with uterine carcinoma who underwent a successful pneumonectomy for metastases ten years after pelvic surgery and two years after the original evidence of pulmonary metastases. Brezina and Lindskog[11] report a similar case with pneumonectomy 13 years after hysterectomy. Tschudi-Madsen[98] had an unusual case of cancer of the uterus. Fourteen years after hysterectomy, roentgenograms showed an infiltration of the right hip. This area was given roentgen ray treatment. Her condition deteriorated but she made a remarkable recovery when treated for pellagra. For four years following, she was in such good condition that the diagnosis of metastasis was questioned. Nineteen years after the hysterectomy she died with extensive metastases to the skeleton. It is considered by some gynecologists that the peritoneal implants of cystic carcinoma of the ovary may regress or remain quiescent after removal of the primary tumor. There are cases in the literature to support this idea such as the report of Olshausen[69] who found local quiescence of 5¼, 7½, 17 and 21 years in four cases after removal of the ovarian tumor. According to Hutcheson,[49] Pemberton[73] had three cases with five, nine and 15 year survival with residual cancer following removal of the primary growth. He also cites Munnell and Taylor who reported 13 cases surviving over five years with one dying 14 years after the original diagnosis. His own case showed metastatic growths in pelvic and iliac regions involving lymph nodes and bone 33 years after removal of the primary cystadenocarcinoma of the ovary. Aimes *et al.*,[1] reported a left retroperitoneal recurrence of a granulosa cell tumor 33 years after right ovariectomy.

In stomach cancers it is not always possible to be sure that a tumor producing a late death is not a new carcinoma in the gastric remnant. However, cases of interest are reported by Shuman,[89] Gould,[37] Persson[75] and Peugniez.[76] These articles include six cases with death more than ten years after surgery, the longest survival being 18 years after partial gastrectomy. Tschetschik and Loewenthal[97] report a case of malignant degeneration of polyposis of the colon with generalized metastases. One area of metastasis in the left lung was present for ten years before the patient died of cerebral metastases. Although teratomas of the testis usually recur rather rapidly, Zerman[105] reports one man who died with metastases 11½ years after orchidectomy and irradiation. This patient was without complaints for over 11 years before developing pulmonary symptoms from metastatic spread.

Whereas the average survival in patients with chronic myelogenous or lymphatic leukemia is about two and a half years,[72] Moffitt and Lawrence[64] report 26 cases with survivals from nine to 25 years. Although most of the patients received the usual treatment, two of the cases survived 16 and 18

years respectively, without any therapy. An eight-year remission is noted by BØe[8] in a patient who died of leukemia 12 years after her original symptoms. Richards and Moench[83] report a case with survival for 16 years without treatment and mention from the literature other cases with survivals of nine to 25 years. They remark that despite the tendency to be gloomy about the prognosis in the leukemias, they may run a comparatively benign course.

It is apparent that there is a wide variation in the resistance of individuals to malignant growths. Consequently, prognosis in terms of survival time in an individual situation should be given cautiously since any case may be well above or below the general average. There is nothing in the records of our patients to indicate the reasons for their long survivals with residual cancers. Gordon-Taylor[35] noted in several cases of recurrent breast carcinoma that evidence of recurrence was first noted following some other illness which lowered the patient's resistance. It is at least possible that the second illness also led to a more critical review of the patient's physical condition. Secondary illness was not a prominent factor in the cases reported here.

It is unfortunate that there is no clue to the reason for the long course of the disease in some patients. If the factors involved were understood, they might supply a lead for more effective handling of the average patient. Perhaps these factors will be found when endocrine balance is more completely understood. There is some evidence from the work of Huggins[47] on the effects of hormone therapy on prostatic cancer that hormonal imbalance may be of great importance, in some types of cancer at least. It has also been shown experimentally by Gardner[32] in mice that the interstitial cells of the testis may remain quiescent in a transplant to a nonestrogenized host for six or seven months. If the animals are given estrogens, these fragments become rapidly growing tumors. Furthermore, recent unpublished work from the Jackson Laboratory suggests that general metastasis of a transplanted cancer may be induced by stimulating the host with frozen dried tumor material combined with injections of cortisone. These are a few of the straws in the wind which may lead to a better knowledge of the control of malignant disease.

SUMMARY

A series of 17 cases of cancers originating in various organs is presented. These cases are unusual in that the patients had long periods of useful survival, although the malignant disease had not been completely eradicated. Because of the differing response of individuals to cancer, the physician should be cautious in estimating the survival of any patient suffering from carcinoma.

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DISCUSSION.—DR. JOE V. MEIGS, Boston, Mass.: I think this is a very important paper. I would like to know whether Dr. Morton is carrying out any immunity studies and whether or not he is trying to find out whether he can boost the resistance of these patients. It is probable that many people have an immunity to disease which may be lost at certain times during their lives. I am sure we have all seen patients with cancer who have gone on for ten or 12 or more years after operation, and then suddenly the cancer may appear in various regions all at once—just as though something that protects them from recurrence is lost. I wanted to ask whether any work is being done in an effort to find out whether there is any immunity against cancer.

DR. J. M. T. FINNEY, JR., Baltimore, Md.: Apropos of what Dr. Meigs just said about immunity, we know that for a long time it was felt that active tuberculosis and cancer did not exist together. I think that has been pretty well disproved. There came to my attention some years ago, via a letter from Asheville, where a man had died of active tuberculosis and on whom autopsy had been performed, a request for the description of an operation which he had had done by my father at Johns Hopkins. I looked up the old history and found that, 17 years previously, he had been operated upon for an adenocarcinoma of the stomach. A large part of the stomach was removed (it was not a total gastrectomy, but a near total one), and there was a note in the operative record that there were several enlarged glands high up under the diaphragm in the gastric mesentery, about 1 cm. in diameter, which felt as though they were involved in the malignant growth. I sent this message back to the doctor at Asheville, and I received in return an autopsy report stating, in substance, "that the stomach showed evidence of having had an extensive resection with no evidence whatsoever of malignancy at the present time; but high up under the diaphragm there are six nodes about 1 cm. in diameter, all of which are almost completely replaced by adenocarcinoma of gastric origin." Seventeen years!

DR. J. ALBERT KEY, St. Louis, Mo.: I thought John had retired. He is a very persistent fellow and, about 30 years ago, he and I used to talk about this subject when we were both much younger. He had been working with Murphy at the Rockefeller Institute and came up to Boston to become an orthopedic surgeon. He failed at that, but I am glad he has not retired intellectually.

I have seen two cases which I can recall, in which I think malignant tumors did not recur, but the patient had another tumor. I think that group has to be separated from this. Undoubtedly, if a statistical study could be made, cases would be found occasionally where the individual exerted natural resistance to tumors, but there would also be individuals who were cured of one tumor and then developed another because they had a natural susceptibility to tumors. I think a study of that type should be included with this study.

DR. JOHN H. MORTON, Rochester, N. Y. (closing): I want to thank the Association for the privilege of closing this discussion, and I want to thank Dr. Meigs, Dr. Finney and Dr. Key for their remarks. So far as studies on immunity and susceptibility in cancer go, these things have interested our group and other groups for many years. Studies are being conducted, but I do not think anything definite can be said as yet.

In addition to the cases we were able to cull from our own files, in the literature there are similar cases, originating in the lung, in bone, in the uterus and ovaries, and in the testes. There are stomach cancers besides the one mentioned by Dr. Finney, and cancers elsewhere in the intestinal tract. There are also many cases of leukemia which show a similar picture. Earlier this evening Drs. Stafford and Ward mentioned a 31 year survival with fibrosarcoma.

I would like to emphasize three points. First, although cases of this type are rare, they do occur and should be remembered when one is offering a prognosis to a patient or a family about carcinoma. Second, as mentioned by Dr. Meigs, in many cases there will be a long period of complete absence of symptoms and then, when the tumor reappears, it spreads very rapidly and the patient succumbs. Third, in these patients we are not talking about people who have just lived and dragged on with carcinoma, but people who have gone on with a long survival of active and useful life.